EXHIBIT A

Immunomedics

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Via Federal Express and Email

September 4, 2018

U.S. Food and Drug Administration
CDER Division of Inspectional Assessment
10903 New Hampshire Avenue
White Oak Building 51, Room 4328
Silver Spring, MD 20993

Attn.: Dr. Mahesh Ramanadham, Director

Re: Initial Response to the Inspectional Observations (Form FDA 483) Dated August 14, 2018

Dear Dr. Ramanadham:

On August 6, 2018, U.S. Food and Drug Administration (FDA) Investigators, Dr. Reyes Candau-Chacon, Dr. Madushini Dharmasena, Dr. Gunther Boekhoudt, and Dr. Rajiv Srivastava, concluded an inspection of Immunomedics' Morris Plains facility, located at 300 The American Road, Morris Plains, New Jersey and issued Inspectional Observations on the Form FDA 483. Enclosed, in duplicate, is the Company's response and corrective action plans.

We recognize, and take seriously, the significance of the observations on the Form FDA 483, and are committed to taking all actions necessary to ensure that our systems are in compliance with FDA requirements, and that our products are safe and effective. As is described in our detailed responses attached, in addition to correcting the specific items listed in the Form FDA 483, we have taken and are continuing to address and implement these corrective actions.

In **Appendix 1**, "Response to the FDA-483 dated August 14, 2018," we describe our completed and planned actions. Supporting documents

related to the completed and planned actions outlined in the responses are included in **Appendix 2**. Please note that, some remediation actions require an extended period of time to address. Therefore, Immunomedics requests that it be permitted to provide interim remediation progress updates to the FDA. In this regard Immunomedics commits to providing progress reports to FDA, by end of each month to include activities completed and accomplished since the previous report.

To facilitate review, the Form FDA 483 observations are in bold text, followed by our response in plain text.

We consider the information contained in this letter and its attachments to be confidential commercial information and not subject to disclosure under the Freedom of Information Act. Accordingly, we have designated this letter and its attachments as confidential.

Should you have any questions, please do not hesitate to contact me at 973-605-8200, ext. 180 or via e-mail at dwhiteley@immunomedics.com.

Sincerely,

Diane Whiteley
Vice President
Regulatory Affairs

cc: Reyes Candau-Chacon
(via email: Maria.Candauchacon@fda.hhs.gov)

Appendix 1: Observations and Actions

In this section, the text of the FDA 483 Observations is in bold text, and the Company response, completed and planned actions are in plain text. Supporting documents related to the completed and planned actions outlined in the responses are included in **Appendix 2**.

Contents

FDA Observation 1

The quality control unit lacks authority to investigate critical deviations of approved procedures. Specifically, the discovery of a data integrity breach in February 2018 did not trigger a deviation. The scope of the data integrity breach included manipulation of bioburden samples, misrepresentation of the (b) (4) integrity test procedure in the batch record and backdating of batch records, including dates of analytical results.

Response:	Immunomedics appreciates the importance of a robust deviation investigation and resolution process as part of an effective quality system, and agrees that it is of the utmost importance that the Quality Unit have the authority to initiate deviations and carry out CAPAs through documented completion. In light of Observation 1, we would like to clarify that the Company's Quality Unit did and does have full authority to investigate deviations and initiate Non-Conformance Report (NCR) forms under our SOPs, including SOP-Q014 Rev. 14: Non-Conformance/Deviation Reporting, Investigation, and CAPA (in effect at the time), and our recent updated SOP-0152: Deviation Handling (effective August 24, 2018). We acknowledge, however, that relative to the matters referenced in Observation 1, our quality documentation did not meet the Agency's expectations in terms of comprehensiveness and timeliness, and will provide our assessment of the root cause of this observation, and our corrective and preventive actions relative to the observation, below. For context on the matters referenced in Observation 1, it is important to clarify the circumstances through which the relevant deviations were alleged and verified, and the Company's prompt and proactive actions in response. As opposed to emerging in manufacturing operations or a routine quality audit, the data integrity issues referenced were identified in a non-routine situation where company personnel came forward describing past misconduct. With respect for "open door" compliance principles and corporate best practices when personnel raise potential compliance concerns, the Company immediately identified the allegations as a matter deserving its utmost attention. The allegations were first raised on Wednesday, January 31, 2018, and in the days immediately following the Company escalated the matter up to the CEO, engaged counsel to investigate the matter with the active and essential support of the Quality Unit, briefed board leadership, and began evaluating potential product and patient impact. As a result of the investigative efforts with the full support of Company leadership, by Monday, (b) (4) the Company had sufficient verification of the allegations to voluntarily notify FDA about these matters. The Company initially disclosed these matters in summary form to FDA in letters dated (b) (4) addressed to Dr. Patricia Keegan, Director, Division of Oncology Products 2 (DOP2), to the attention of Ms. Leah Her, MS, Regulatory Health Project Manager for (b) (4) The investigative effort continued and the Company submitted a follow-up voluntary notification to the relevant (b) (4) on (b) (4) (b) (4) which identified that other matters with a common root cause (employee misconduct) had been detected, and that a number of remedial measures had been and were being taken. The Company's assessment was that the employee misconduct identified and verified—while of significant concern, and to a level triggering prompt action including the separation of three managers from the Company—did not impact finished product quality or (based on a health hazard evaluation which was submitted

	to the agency and a risk assessment document, TR-QC-IMMU-132-18-012: "Assessment of the Risk Arising from Pre and Post Use Testing of (b) (4) (b) (4) During Purification of (b) (4) present a health risk to those taking the finished product. For clarification regarding Observation 1, the Company's Quality Unit did document deviations that were deemed to have a potential for product quality impact under the Company's Non-Conformance Report (NCR) process: deviations in connection with the mishandling of Bioburden and Endotoxin samples (18-009U) and improper (b) (4) integrity testing of the (b) (4) (18-053U). These deviations were reviewed by FDA investigators during the inspection. The Company acknowledges, however, that the Quality Unit did not initiate these NCRs at the beginning of the investigation. Below we explain the measures we have taken and will take to correct where possible the observed circumstances, and to prevent the recurrence of these or similar circumstances.
Completed Actions:	The Company has issued an Ethical Conduct and Data Integrity corporate policy (**Appendix 2, Attachment 1**), initiated a Data Governance Program (**Appendix 2, Attachment 2**) and provided training on data integrity and good documentation practices to all pertinent staff, with completion certified by signature. The Deviation Handling SOP (SOP-0152) has been updated to ensure a deviation is initiated (b) (4) of identification. Staff training on this SOP has been completed, with completion certified by signature.
Planned Actions:	The Company considers this item to be closed.

FDA Observation 2

There is no assurance that samples and batch records from the (b) (4) intermediate process validation and commercial batches manufactured prior to February 2018 were not impacted by the data integrity breach. Interviews by Immunomedics to personnel involved in the event were conducted under attorney/client privilege and no additional documentation is available, therefore no assessment could be made during the pre-license inspection in support of (b) (4)

Response:	Immunomedics acknowledges this observation. Due to placing the investigation of the data integrity breach under Attorney Client Privilege, it was difficult for the FDA investigators to assess the impact of the data integrity breach. Immunomedics would like to emphasize that immediately upon discovery of this issue, the Company submitted multiple communications to FDA updating the center on the progress of the investigation including a Health Hazard Evaluation (HHE). The communications were dated (b) (4) and (b) (4) and included a HHE, as stated. Additionally, during the inspection, a completed risk assessment report was shared with FDA investigators. Subsequent to the inspection, in response to (b) (4) (b) (4) a summary of the risk assessment was also submitted. The HHE and the Risk Assessment clearly demonstrate that the manufacturing process for the (b) (4) intermediate provides sufficient assurances that PPQ manufactured batches carry a very low patient safety risk. The risk assessment concludes that the technical merits of the process validation studies were not adversely impacted to the extent which would render Drug Product derived from the (b) (4) manufacturing process a risk to patient safety or, in any way invalidate the key technical findings of the process validation study. Furthermore, as stated in the response to (b) (4) the Company has made a commitment to conduct additional testing of (b) (4) intermediate batches for (b) (4) as requested by the Agency. For more details, please see response to (b) (4) (**Appendix 2, Attachment 3**). Immunomedics acknowledges the importance of compliance to cGMPs and have a zero-tolerance policy for data integrity breaches from a corporate and ethical perspective. As mentioned in response # 1, the Company has implemented a corporate ethical conduct and data integrity policy and data governance program. All PPQ batches remain "on hold" pending acceptability of the (b) (4)
Completed Actions:	• Health Hazard Evaluation dated (b) (4), submitted to FDA • Risk Assessment for (b) (4) Process Report #TR-QC-IMMU-132-18-012, dated July 6, 2018 • (b) (4) a summary of the risk assessment Issued an Ethical Conduct and Data Integrity Policy (POL-0018) and Data Governance Program (POL-0019) and completed training of staff.
Planned Actions:	Additional testing for (b) (4) will be performed on (b) (4) intermediate batches as described in (b) (4) **Target Completion Date:** December 31, 2018

FDA Observation 3

Retesting procedure for the (b) (4) intermediate is inadequate. Specifically:

A. SOP-0162 "Out of Specification Investigations" indicates that "if the company believes there is possibility the laboratory test did have error, and the error was undetected, then the company may wish to perform a retest." OOS Investigation report 18-001 shows that routine retesting was performed due to an initial OOS result.

Response:	As discussed during the Pre-Approval Inspection, we acknowledge that SOP-0162, the Out of Specification (OOS) procedure, should be revised and we will do so under Document Change Control-000464 to clarify that retesting is not permitted in response to an initial OOS test result on a discretionary basis but only if specific criteria are met. The modified procedure will follow FDA's guidance document on "Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production" and will specify that retesting procedures may only be allowed after a test plan, supported by sound scientific judgment is approved by the Head of Quality. The test plan will describe the testing to be performed and the scientific and/or technical handling of the data. The modified procedure will also require that unconfirmed OOS results are documented and thoroughly investigated to either substantiate or rule out any possible error.
Completed Actions:	Our actions in response to Observation 3A are in process.
Planned Actions:	The OOS Procedure (SOP-0162) will be modified under Document Change Control-000464 to clarify that retesting may only be allowed under strictly defined conditions that are consistent with FDA guidance. **Target Completion Date:** September 28, 2018

B. Specifically: SOP-0162 allows for retesting of microbiology samples. An OOS result for the (b) (4) (b) (4) in-process bioburden sample was recorded on 12/23/2017. A retest was conducted using a retain sample on 1/5/2018 and the results on 1/10/2018 were OOS (OOS 18-001). Initiation of a non-conformance report (NCR 18-009U) was delayed until the results of the retest were reported on 1/10/2018.

Response:	We acknowledge the deficiencies in the handling of this retesting procedure and the delay in the NCR initiation.
Completed Actions:	Our actions in response to Observation 3B are in process.
Planned Actions:	The Company has opened CAPA 18-034 to conduct and document a review of all bioburden test results starting with the initiation of the PPQ campaign (Aug-2017) to present. The impact of any occurrences of retesting of microbiological samples will be assessed and included in a summary report under the CAPA. **Target Completion Date:** September 28, 2018 The OOS Procedure (SOP-0162) will be revised under Document Change Control-000464 to specify that OOS results from bioburden testing are a deviation. In addition, as reviewed with the Inspection team during the Pre-Approval Inspection, the practice of resampling for microbiology testing (Change Control 18-177P) will be eliminated. **Target Completion Date:** September 28, 2018

FDA Observation 4

The raw material sampling and testing program is inadequate.

Response:	Immunomedics recognizes the importance of enhancing the control of the raw material sampling and testing program.
Completed Actions:	The Supplier Qualification Program (SOP-0148, **Appendix 2, Attachment 4**) has been updated to provide additional criteria for the selection of raw materials, supplier approval process, quality agreements and supplier qualification. A new SOP (SOP-0698, **Appendix 2, Attachment 5**) has been created to describe the GMP Raw Material Qualification Program, which involves sampling and testing of the raw material prior to being released for us in manufacturing. As part of SOP-0698 each material, based on quality attributes and material risk assessment, will be fully tested according to the Certificate of Analysis each time the material is received. A raw material may qualify for reduced testing, when three (3) consecutive lots are fully tested and documented as passing and the supplier qualification process has been completed. Per SOP-0698, (b) (4) full testing is required to maintain the reduced testing status. The Sampling of Raw Materials SOP (SOP-0185, **Appendix 2, Attachment 6**) has been revised to include a statistically justifiable sampling (ANSI/ASQ z1.4), testing, and retention program.

Planned Actions:	The Company will implement a GMP Raw Material Sampling and Testing Program. This action will be tracked under CAPA 18-004. **Target Completion Date:** December 31, 2018

Specifically:

A. (b) (4) solution (b) (4) supplied by (b) (4) has never been sampled and there is no assurance that the manufacturer can consistently provide material meeting specifications. The solution is (b) (4) sterilized from the vendor and is added unfiltered to the cell culture bioreactors. Deviations 18-081U and 18-163U were initiated due to contamination in the (b) (4) bioreactors. In both cases, probable root causes included the (b) (4) addition assembly (b) (4) bag, line and valve). Testing of an unused (b) (4) bag in inventory also resulted in a positive sample.

Response:	Recognizing the importance of ensuring sterility of the (b) (4) Immunomedics will implement sterility testing on each lot of (b) (4) solution (b) (4) prior to the lot being released for use in manufacturing.
Completed Actions:	Our actions in response to Observation 4A are in process.
Planned Actions:	Immunomedics will perform full testing on each lot of (b) (4) solution in accordance with the supplier Certificate of Analysis as part of qualification of the raw material detailed in Response 4 above unless and until it meets the criteria for reduced raw material testing under SOP-0698. **Target Completion Date:** November 30, 2018

B. Product-contact (b) (4) and (b) (4) used during cell culture of the (b) (4) intermediate are not tested for bioburden.

Response:	Immunomedics acknowledges the deficiency and agrees to test product-contact (b) (4) and (b) (4) for viable count and total particulate counts. The (b) (4) and (b) (4) are utilized to maintain pH and the appropriate dissolved (b) (4) levels within the culture, respectively.
Completed Actions:	Our actions in response to Observation 4B are in process.
Planned Actions:	To mitigate any potential for risk to the process and to ensure quality, each of the above (b) (4) will be evaluated for both viable and total particle count as part of material qualification. Post qualification, incoming (b) (4) will be tested for identification and viable and total particle count prior to release. Immunomedics to initiate testing following qualification of vendor to conduct testing. **Target Completion Date:** December 31, 2018

FDA Observation 5

The firm lacks procedures for inventory audit trail and for tracking and reconciliation of raw materials used to manufacture the (b) (4) intermediate. Specifically:

A. **The firm does not keep records tracing the use of raw material. Raw material reconciliation cannot be conducted as discarded raw materials are not documented. During the tour to the manufacturing facility on 8/6/2018, the inspection team observed a (b) (4) L container of (b) (4) (b) (4) in the loading dock for destruction. The material could not be traced.**

Response:	Immunomedics acknowledges the deficiencies in inventory control noted during the Pre-Approval Inspection and commits to resolve each deficiency. Immunomedics is taking steps to improve our record keeping systems to support reconciliation of materials received and used. Understanding the criticality of Inventory Control, Immunomedics has signed an agreement with a vendor to support implementation of a computerized inventory system to track and monitor the movement of raw materials.
Completed Actions:	Immunomedics utilizes Form FRM-0157: Material Usage Card designed to manually record and track the movement of raw materials from the GMP warehouse (Building 410) to other processing areas (Quality, Manufacturing, Research & Development) located in Building (b) (4). The Material Usage Card will continue to be the primary reconciliation of materials received until the Company's electronic inventory system is online and validated in December 2018.
Planned Actions:	Immunomedics is implementing additional processes for reconciling all materials transferred to Manufacturing in Building (Bldg.) (b) (4) Currently, Quality creates a Material Usage Card for receipt of every controlled material. When material is distributed to Bldg. (b) (4) the transfer is recorded on the Material Usage Card maintained in Bldg. 410. Each material transfer will include a Manufacturing Usage Card which will be used by the recipient in Bldg. (b) (4) to record and reconcile the amount received, identify amount used, where/when used and or discarded until the received quantity is completely accounted for. Once reconciled, the Bldg. (b) (4) Material Usage Card is matched with the Bldg. 410 Manufacturing Usage Card to have a complete reconciliation of materials used. Reconciliation of the Material Usage Card and Manufacturing Usage Card is the responsibility of the Supply Chain Department. **Target Completion Date:** October 31, 2018 The computerized ERP Inventory Control module is scheduled to go online in December 2018. Until the ERP Inventory system is online and validated, Immunomedics will continue utilizing the manual reconciliation process, i.e., Location Tracking Report and Material Usage Card. **Target Completion Date:** December 31, 2018

B. Warehouse raw material inventory list is kept in an Excel Spreadsheet that lacks history traceability. During the tour of the warehouse on 8/6/2018 Warehouse inventory cannot be located using the Excel Spreadsheet. Specifically, (b) (4) (catalog #(b) (4) Lot (b) (4) was present in the warehouse, however the location and inventory could not be provided.

Response:	During the Pre-Approval Inspection Immunomedics provided a copy of the Location Tracking Report which identifies the location and quantity of each material stored in the GMP warehouse (Bldg. 410). The Location Tracking Report is printed (b) (4) The report is manually updated by warehouse operators to reflect any movements, additions or deletions of materials. Once the (b) (4) movements are complete and recorded on the report, the report is updated, and a new copy is printed to support the (b) (4) transactions. All copies of the Location Tracking Report are retained for history/traceability of movements within the warehouse.
Completed Actions:	Interim measure: Process implemented
Planned Actions:	Location Tracking Report work instruction is in development. **Target Completion Date:** September 30, 2018 The computerized ERP Inventory Control module is scheduled to go online in December 2018. Until the ERP Inventory system is online and validated, Immunomedics will continue utilizing the manual reconciliation process, i.e. Location Tracking Report and Material Usage Card. **Target Completion Date:** December 31, 2018

C. The warehouse is not adequately mapped for inventory purposes with floor plans. Items stored on the floor have no assigned location. In addition, quarantine and released items on the floor are kept side-by-side without a system in place to prevent the use of quarantined raw material.

Response:	To prevent the potential of quarantine material being used, Immunomedics will utilize visual control for usage of approved materials. No materials will be used by manufacturing unless labeled with the appropriate "Approved" or "Conditional Release" label.
Completed Actions:	With the implementation of the Location Tracking Report described in Response 5b, a detailed map of locations, including floor sections (L/K/J) was created (**Appendix 2, Attachment 7**). Approved and quarantined materials have been segregated by locating material with a single status per warehouse floor section (L/K/J) at any given time. All product in a specific warehouse floor section have been accounted for and designated as either approved or quarantine. To further prevent the potential of using quarantine material, the warehouse has racks labeled with Approved and Quarantine. Reject material is placed in a fenced-locked area. Any floor area used for storage are clearly segregated to identify the material as quarantine or approved. As described above, Immunomedics has signed an agreement with a vendor to support implementation of a computerized inventory control system.
Planned Actions:	The computerized ERP Inventory Control module is scheduled to go online in December 2018. Until the ERP Inventory system is online and validated, Immunomedics will continue utilizing the manual reconciliation process, i.e. Location Tracking Report and Material Usage Card which will be the responsibility of supply chain. **Target Completion Date:** December 31, 2018

FDA Observation 6

Differential pressure between GMP areas of different area classification is not adequately maintained and monitored.

Response:	Immunomedics acknowledges that differential pressure between controlled areas with different area classifications has not been adequately maintained and monitored. Pressure differentials to assure protection of product through an appropriate (b) (4) has been maintained throughout production of clinical and commercial lots. Historically, the monitoring of pressure differentials has been performed through manual monitoring of magnehelic pressure gauges. In January 2018, Immunomedics authorized a project to install a new (b) (4) environmental monitoring system. This system provides continuous monitoring of the critical area parameters including pressure differential, temperature and humidity and will also monitor conditions in the temperature-controlled storage areas.
Completed Actions:	(b) (4) (b) (4) performed a preliminary review of the documentation of from the most recent production campaign. Their findings were that the differentials between areas of differing classification meet or exceed guidance values (10-15 Pa).
Planned Actions:	Complete final set-up, training and qualification of the (b) (4) environmental monitoring system. Establish appropriate set-points for alert and alarm action levels. Update SOPs for managing alarm responses. Enhance the existing pressure differential monitoring procedure to ensure timely review of differential pressure readings and issuance of deviations, as required. **Target Completion Date:** December 31, 2018

Specifically:

A. Air pressure in the GMP areas is not adequately maintained. For example, differential pressure between Rooms (b) (4) (Class C (b) (4) suite (b) (4) and (b) (4) (Class D corridor) was out of action levels in 37 out of (b) (4) measurements between July 24, 2018 and August 1, 2018.

Response:	Immunomedics is conducting a review of all manual readings from the start of the PPQ campaign to present (August 2017 – July 2018) and appropriately assess deviations and conduct investigations as needed.
Completed Actions:	The following controls were in place to mitigate the impact of any deviations: • (b) (4) with the highest pressures in rooms where critical operations are performed were maintained to protect product, according to HVAC balancing reports and filter certification. • Sanitization was performed (b) (4) per SOP–0076 using (b) (4) (b) (4) and (b) (4) using (b) (4) to ensure maximum bioburden control. • Static and dynamic environmental monitoring for total and viable particulate was conducted per SOP-0275. A review showed all results to be within established specifications. • Operators were retrained and recertified in controlled area gowning practices. • HEPA filters were tested (b) (4) and passed integrity testing. The last date tested was April 2018
Planned Actions:	The Company will complete review of all manual magnehelic pressure readings from the start of the PPQ campaign to present (August 2017 – July 2018) and appropriately assess deviations and conduct investigations as needed. **Target Completion Date:** October 31, 2018

B. Continuous monitoring of pressure in the GMP areas has been installed in July 2018 and is undergoing qualification, however not all adjacent rooms with different air classification are alarmed for low pressure differential. For example, differential pressure between the Rooms (b) (4) (b) (4) (Class C (b) (4) suite (b) (4) and (b) (4) (Class D corridor) is not alarmed.

Response:	A review of our current installation indicated that with the exception of the above-mentioned (b) (4) to corridor, the monitoring points are all adequate to monitor and alarm differential pressure between ISO classifications and critical room (b) (4)
Completed Actions:	Our actions in response to Observation 6B are in process.
Planned Actions:	A sensor will be installed in Room (b) (4) to provide continuous monitoring of pressure differentials and alarming between Room (b) (4) and Room (b) (4) This addition will provide monitoring and alarming across all Grade C and Grade D classifications. **Target Completion Date:** September 28, 2018

FDA Observation 7

The design of the facility is inadequate in that no drains are present in the purification rooms. In addition, there is no SOP for liquid containment and disposal after a catastrophic spill. All process streams downstream the (b) (4) Bioreactor are held in disposable bags.

Response:	Immunomedics recognizes the importance of providing adequate spill protection in the areas utilizing (b) (4) bags for transfer of product, however the Company contends that the lack of drains in the purification area does not make the facility inadequate for its intended purpose. In designing the purification suites, the decision to not install drains will permit the tightening of room classifications beyond Class "C" (ISO level 8), if required, per The Eudralex Volume 4 Annex 1 guidelines to ensure Immunomedics meets bioburden requirements on a global level.
Completed Actions:	Our actions in response to Observation 7 are in process.
Planned Actions:	While the purification facility does not have drains, Immunomedics will assemble an appropriate spill control kit containing the necessary equipment to quickly control any spill up to the (b) (4) L contained in the transfer bags. A detailed SOP will be developed, and production personnel trained to utilize equipment to contain any spill and initiate an appropriate response from management and environmental health and safety. **Target Completion Date:** October 31, 2018

FDA Observation 8

There is no signed Quality Agreement between (b) (4) and Immunomedics Inc. (b) (4) is the supplier of cell culture media and all (b) (4) solutions (including (b) (4), and (b) (4) used for (b) (4) purification of the (b) (4) intermediate.

Response:	Following Immunomedics SOP-Q010: Vendor Qualification/External Audit Program, the (b) (4) facility in (b) (4) was audited on 08 Nov 2017 as a supplier of critical materials (cell culture media, (b) (4) and (b) (4) The outcome of this facility confirmed (b) (4) (b) (4) as a qualified supplier for these critical materials. The facility where the (b) (4) are manufactured is located in (b) (4) An audit of the (b) (4) facility is scheduled for 25 Oct 2018. These (b) (4) facilities are governed by the overarching Quality Agreement. Furthermore, we recognize the importance of a robust vendor quality management program and are in the process of putting in place quality agreements and conducting audits as outlined below under Planned Actions.
Completed Actions:	A Quality Agreement between (b) (4) and Immunomedics was fully executed on 07 Aug 2018 and provided to the investigation team on August 8, 2018.
Planned Actions:	CAPA 18-004 discussed during the inspection, outlines the plan for all quality agreements with Critical Level 1 Suppliers to be fully executed by March 29, 2019. Additionally, as part of the Vendor Qualification Program, all levels of vendors (i.e., Levels 1, 2 and 3) will have current Quality Agreements or equivalent Quality Statements established. **Target Completion Date:** March 29, 2019

FDA Observation 9

No procedure is in place for (b) (4) intermediate (b) (4) trending of results. During the process validation (PPQ) campaign, bioburden levels in the (b) (4) were not trended and inadequately high bioburden levels were not investigated. Low level bioburden (29 to 186 CFU/100 mL) was observed in the (b) (4) after sanitization in PPQ batches (b) (4) and the bioburden level increased to too numerous to count in PPQ batch (b) (4) No deviation was initiated.

Response:	Immunomedics Manufacturing and Quality Assurance are in the process of establishing a continuous process improvement program that will be used to monitor and improve the (b) (4) intermediate (b) (4) manufacturing activities. This will be one component of a broader program to monitor and improve (b) (4) manufacturing throughout the entire supply chain. An initial process control strategy (PCS) for (b) (4) has been prepared based on Process (b) (4) and the recently completed process validation studies. The PCS will serve as the basis for establishing a data monitoring program for the intermediates and products produced at Immunomedics as well as at our contract manufacturing partners. Data monitoring, in conjunction with continued process verification (CPV), will utilize the manufacturing and supporting data, (e.g., QC and QC micro) for periodic re-evaluation of the process parameters and attributes identified in the PCS, and provide a basis for appropriate statistical process control (SPC) and trending analysis of manufacturing activities. Supporting documentation (SOPs) will be established to delineate the data gathering (mining) and storage methods (compliant with data integrity initiatives), data analysis methods, reporting and review requirements for the data, and documentation of the results of the program on a periodic basis. The program will be initiated in September 2018 with data mining of the PPQ campaign and subsequent data to populate the database. Concurrent with the data mining efforts, SOPs will be drafted and approved by October 2018, allowing an initial periodic product quality review (PPQR) in November 2018, at which time sufficient data will be available for a meaningful review. The PPQR meetings are planned to occur approximately (b) (4) and cumulatively, serve as the basis for the annual product review (APR). SOPs that will be developed include: • Data Gathering- delineating the data to be collected, stored and data integrity requirements for the database; • Data Monitoring- establishing the content, attendees, and frequency for data monitoring reviews at the local/team level; • Data Trending- establishing the expectations/requirements for statistical process control, statistical analysis, trend recognition, capability analysis, and associated methodologies for data monitoring and analysis; • PPQR- establishing the requirements for the frequency, content, and attendees at the PPQR meetings; and

	• APR- an existing SOP will be evaluated and modified as necessary and appropriate.
Completed Actions:	Our actions in response to Observation 9 are in process.
Planned Actions:	Initiate data mining activities Develop SOPs outlining: • Data Gathering- delineating the data to be collected, where it is to be stored, data integrity requirements for the database; • Data Monitoring- establishing the content, attendees, and frequency for data monitoring reviews at the local/team level; • Data Trending- establishing the expectations/requirements for statistical process control, statistical analysis, trend recognition, capability analysis, and associated methodologies for data monitoring and analysis; • PPQR- establishing the requirements for the frequency, content, and attendees at the PPQR meetings; and • APR- evaluate existing SOP and modified as necessary. and appropriate. Conduct PPQR meeting **Target Completion Date:** November 30, 2018

FDA Observation 10

Deviation investigations and CAPA implementations are inadequate.

Response:	Immunomedics is developing a remediation plan to comprehensively and holistically improve cGMP compliance across all quality systems, processes and procedures. The goal will be to define a quality system that supports quality and operational processes and drives continuous improvement across the Company. Immunomedics plans to make systemic enhancements that will lead to broad based improvements in system controls, system operations and system effectiveness. In support of this plan, Immunomedics commits to re-designing various elements of the Quality System, including deviation handling and CAPA procedures.
Completed Actions:	Our actions in response to Observation 10 are in process.
Planned Actions:	The Company's systemic improvements to its Quality System include the re-design of the Deviation and CAPA management processes. These changes include (but are not limited to): • Establishing timelines for initiation of deviations, implementation and documentation of containment actions and development of interim reports for deviations requiring additional time for closure • Performing investigations by staff qualified in conducting investigations • Enhancing the investigation process by incorporating investigative plans, CAPA plans and identification of interim control measures • Including requirements for lot specific impact assessment • Including requirements for documented risk assessments • Including requirements for assessment by Quality Assurance of evidence of CAPA implementation and effectiveness • Defining the use of Root Cause analysis tools to support the investigation process **Target Completion Date:** December 31, 2018

For example, Deviation 18-053U was initiated after an internal audit concluded that the (b) (4) had not been adequately tested for integrity pre- or post-(b) (4).

A. Lot number in the deviation form indicates "multiple lots" without specifying the potential lots impacted.

Response:	Deviation 18-053U was non-routine, as it was initiated in relation to allegations verified through counsel's investigation (discussed in the response to Observations 1 and 2) and Quality concluded that all lots processed were potentially impacted by the event. We recognize, however, that as documented this reference appeared imprecise, and agree that the specific lot numbers should have been listed.
Completed Actions:	Deviation 18-053U has been amended to include a list of lots impacted or potentially impacted by this deviation (**Appendix 2, Attachment 8**). Further, a "Protocol for Retrospective Review of Major and Critical Deviations and CAPA Relevant (b) (4) Intermediate Bulk PPQ Lots" (**Appendix 2, Attachment 9**) has been approved to ensure previously closed Deviations include lot-specific impact assessments.
Planned Actions:	The Company will fully execute the "Protocol for Retrospective Review of Major and Critical Deviations and CAPA Relevant (b) (4) Intermediate Bulk PPQ Lots". As required, deviations will be amended to include full impact assessment. **Target Completion Date:** November 30, 2018 The Company will improve its Quality System including the re-design of the Deviation and CAPA management processes. **Target Completion Date:** December 31, 2018

B. Product impact assessment includes the conclusion of a clinical Health Hazard Assessment, but no risk assessment on the presence of (b) (4) in the product is documented.

Response:	An "Assessment of the Risk Arising from Inappropriate Pre- and Post-Use Testing of (b) (4) During Purification of (b) (4) was approved on July 6, 2018. This risk assessment determined that the materials in question carry a low safety risk from potential (b) (4) contamination. It is acknowledged the risk assessment should have been included as part of Deviation 18-053U prior to closure.
Completed Actions:	Deviation 18-053U has been amended to include the risk assessment on the presence of (b) (4) in the product (**Appendix 2, Attachment 8**). A "Protocol for Retrospective Review of Major and Critical Deviations and CAPA Relevant (b) (4) Intermediate Bulk PPQ Lots" (**Appendix 2, Attachment 9**) has been approved to review and ensure previously closed Deviations include a risk assessment, as applicable.
Planned Actions:	The Company will fully execute the "Protocol for Retrospective Review of Major and Critical Deviations and CAPA Relevant (b) (4) Intermediate Bulk PPQ Lots". As required, deviations will be amended to include a risk assessment.

	Target Completion Date: November 30, 2018

C. For example, Deviation 18-053U was initiated after an internal audit concluded that the (b) (4) (b) (4) had not been adequately tested for integrity pre- or post- (b) (4) . Deficiency C: The CAPA section indicates that remediation included "...purchasing additional test equipment to evaluate the (b) (4) pre & post its use." However, at the date of the inspection no additional equipment has been purchased and no information about the CAPA is documented in the deviation.

Response:	Deviation 18-053U was closed in April 2018. At the time there was no system in place to monitor completion of Corrective and Preventive Actions (CAPAs). In June 2018, Immunomedics implemented a new CAPA procedure SOP-0652 (**Appendix 2, Attachment 10**). The procedure requires assignment of CAPA tracking numbers, an owner and due dates for each action outlined in the deviation. A designated Quality Assurance staff member monitors CAPA progress to ensure timely completion of actions. Further, CAPA effectiveness checks have been instituted and evidence of CAPA completion and effectiveness is required. Immunomedics is committed to sustainable compliance and currently requires metrics for on time CAPA completion as part of the Immunomedics Quality Council Charter (**Appendix 2, Attachment 11**) to monitor quality system health. The "Protocol for Retrospective Review of Major and Critical Deviations and CAPA Relevant (b) (4) Intermediate Bulk PPQ Lots" (**Appendix 2, Attachment 9**) includes verification of CAPA actions. Any pending actions will be added to the current CAPA monitoring system to ensure closure.
Completed Actions:	Actions were taken to implement the CAPA for the acquisition of new (b) (4) test equipment. While investigating alternatives for automated testing of the (b) (4) (b) (4) the (b) (4) manufacturer, (b) (4) informed Immunomedics that the standard instruments available for (b) (4) integrity testing did not perform well for testing of the (b) (4) Based on this information, the actions were redirected to further collaborate with (b) (4) to improve the testing methodology. These actions included staff training on the (b) (4) i recommended method for integrity testing of the (b) (4) . The initial training occurred in March 2018. Additional training, using (b) (4) that pass and fail integrity testing will be conducted in September 2018. Subsequent to training applicable procedures will be updated.
Planned Actions:	Conduct (b) (4) integrity testing **Target Completion Dates:** September 28, 2018 Conduct additional (b) (4) integrity test training. Update to (b) (4) integrity test procedure. **Target Completion Dates:** November 30, 2018

FDA Observation 11

Deviation initiation and closing times are inadequate.

Response:	Immunomedics acknowledges the deviation procedure has not been consistently followed. As discussed during the Pre-Approval Inspection, Immunomedics is fully committed to establishing a first-class quality system. Immunomedics commits to implementing the Deviation and CAPA management processes. These changes include (but are not limited to): • Defining timelines for initiation of deviations, implementing and documenting containment actions and development of interim reports for deviations requiring additional time for closure • Performing investigations by staff qualified in conducting investigations • Enhancing the investigation process by incorporating investigative plans, CAPA plans and identification of interim control measures • Including requirements for lot specific impact assessment • Including requirements for documented risk assessments • Including requirements for assessment by Quality Assurance of evidence of CAPA implementation and effectiveness • Defining the use of Root Cause analysis tools to support the investigation process
Completed Actions:	As an initial step to accomplish this goal Quality Assurance leadership provided coaching and mentoring to staff on: • Assessing events for proper management notification/escalation, • Properly documenting deviations, • Procedures on prioritization of activities to escalate and address critical and major events in a timely manner while directing resources to close overdue records. Immunomedics implemented enhancements to the Deviation Handling SOP-0152 to clearly establish requirements for notification to Quality Assurance within (b) (4) (b) (4) from discovery. These requirements will ensure that all events are reported to Quality Assurance in a timely manner. New requirements for completion of interim reports with extension justification for records that cannot be closed in (b) (4) have been implemented. In addition, the Deviation Form has been enhanced to provide clarity regarding timing for completion of different steps of the investigation process. As part of the mechanisms in place for management oversight of Deviations is the Deviation Review Board, consisting of the Head of Quality and functional Directors. This forum provides leadership in prioritization of activities to support timely closure of deviations, defines investigative plans to ensure all required elements are included in deviation reports and provides coaching and mentoring to deviation leads during the investigation process. For sustainable compliance a re-organization of the Quality unit has been approved to include a Deviation/CAPA Manager with dedicated resources to ensure timely closure of deviations as well as ensuring all required elements are properly documented. Recruiting for the Deviation/CAPA Manager is in progress.

Planned Actions:	Closure of all overdue Deviations. Hire Deviation/CAPA manager within Quality unit. **Target Completion Date:** December 31, 2018

A. SOP-0152 "Deviation Handling" indicates that if the deviation cannot be completed by the assigned due date, a one-time extension can be requested to the QA unit. The following deviations were not closed by the due date and did not include an extension:

- **i. 18-116U: deviation due was 7/20/2018; deviation was open at the time of the inspection**
- **ii. 18-081U: deviation due date was 6/17/2018; deviation was open at the time of the inspection**
- **iii. 18-079U: deviation due date was 6/16/2018; deviation was closed on 8/3/2018**
- **iv. 18-050U: deviation due date was 5/9/2018; deviation was open at the time of the inspection**

Response:	Immunomedics acknowledges the deviation procedure has not been consistently followed. As discussed during the Pre-Approval Inspection, Immunomedics is fully committed to establishing a first-class quality system. Immunomedics commits to implementing a Deviation management process to include new requirements for completion of interim reports with extension justification for records that cannot be closed in (b) (4)
Completed Actions:	An interim report has been completed for Deviations 18-116U and 18-081U. These reports included all facts known to date, preliminary impact assessment, interim controls to mitigate risk and extension of due date justification. Deviation 18-050U was closed on August 3, 2018.
Planned Actions:	Please refer to the additional broader planned actions regarding Deviations noted in Response 11. **Target Completion Date:** December 31, 2018

B. SOP-0152 "Deviation Handling" does not specify a time limit between time/discovery of event and deviation initiation. The following observations were initiated more than one month after event discovery:

- **i. 18-009U: investigation into bioburden OOS #18-001 for (b) (4) date of event was 1/10/2018, deviation was initiated on 3/27/2017**
- **ii. 18-053U: (b) (4) related discrepancy; date of event was February 2018, deviation was initiated on 4/9/2018**

Response:	Immunomedics recognizes the need for improving the Deviation Handling SOP-0152 to specify a time limit between discovery of the event and deviation initiation.
Completed Actions:	The Deviation procedure was revised and made effective on August 24, 2018 specifying (b) (4) from discovery to notification to Quality and Deviation initiation. To heighten awareness of the importance of promptly reporting and documenting deviations, a training session including the Manufacturing, Quality Assurance and Quality Control management team was conducted on August 15, 2018.
Planned Actions:	The Company considers this specific observation closed. Please refer to the additional broader planned actions regarding Deviations noted in Response 11. **Target Completion Date:** December 31, 2018

FDA Observation 12

Cleaning of downstream equipment, including (b) (4) and product-contact parts of the (b) (4) (b) (4) is not validated or verified. Non-conformance report 18-009 initiated due to a (b) (4) OOS bioburden sample includes as the primary root cause the (b) (4) contaminated during vendor (b) (4) testing.

Response:	Immunomedics, Morris Plains facility is a (b) (4) dedicated facility manufacturing (b) (4) drug component that is further manufactured into (b) (4) (b) (4) The current validated downstream manufacturing process has several engineering and in-process controls to ensure cleaning/ sanitization of the downstream equipment and to monitor and control bioburden and endotoxin levels throughout the purification process. The purification process takes place in a class C environment with a limited access to the personnel who have been specifically trained on the gowning practices and aseptic techniques to minimize any contribution to the bioburden levels in the area. As per the current procedure SOP-0134, (b) (4) is sanitized (b) (4) with (b) (4) for (b) (4) and each of the (b) (4) are also sanitized (b) (4) with (b) (4) for (b) (4) or (b) (4) for (b) (4) as part of manufacturing procedures MP-54901, MP-54902 & MP-54903 respectively. Based on the (b) (4) article, (b) (4) Application note, (b) (4), even with (b) (4) and exposure for (b) (4) (b) (4) is effective in inactivating a number of yeasts and bacteria with log reduction ranging from 3.5 – 8.1 (**Appendix 2, Attachment 12**). Additionally, Immunomedics has several existing in-process controls to monitor and control bioburden and endotoxins as listed below: • During the (b) (4) pH and conductivity samples are taken to verify that the sanitization solution has been completely removed. • Bioburden and endotoxin samples are taken from (b) (4) during the (b) (4) post sanitization. • In-process samples are taken for bioburden and endotoxins and tested to meet the in-process acceptance criteria. • Post storage samples are taken for (b) (4) (b) (4) for bioburden and endotoxin samples. (b) (4) is sanitized (b) (4) and stored in (b) (4) (b) (4) to prevent any bioburden increase. A recent procedure change was made to move the (b) (4) and (b) (4) sanitization from (b) (4) (b) (4) eliminating the (b) (4) hold time in (b) (4) (b) (4) for the system.

	Components of the (b) (4) systems are washed and (b) (4) prior to use in the purification process thus controlling the bioburden level in the process. Additionally, all incoming (b) (4) are also monitored for bioburden.
Completed Actions:	Our actions in response to Observation 12 are in process.
Planned Actions:	As part of continuous improvement program, Immunomedics will execute a comprehensive cleaning validation program for the (b) (4) purification process. This program will include the following elements and studies. 1. Cleaning validation will be executed for the (b) (4) and samples will be for total organic carbon (TOC) -swab and rinse, bioburden and endotoxins. 2. The cleaning process of (b) (4) (b) (4) will be validated as part of the life time studies and will also include (b) (4) (b) (4) to evaluate any carry over. 3. Currently (b) (4) are dedicated to a single product. This approach will be further enhanced by dedicating (b) (4) to specific (b) (4) Visual verification after rinsing to assure absence of (b) (4) particles (easily visible); exchange of wear & tear parts prior to re-assembly/packing. 4. Cleaning validation will be executed for the (b) (4) associated with (b) (4) operations and samples taken for TOC rinse, endotoxins and bioburden. 5. All (b) (4) components are currently being washed in a washer. The cleaning validation of the washer is ongoing and will be completed as per the manufacturing schedule. **Target Completion Date:** March 29, 2019

FDA Observation 13

The procedure to prevent contamination of the (b) (4) intermediate after (b) (4) is inadequate for a product stored 2 to 8°C for up to (b) (4)

Response:	The operations observed and discussed in Observation 13 are conducted in a Grade C area relative to aseptic processing, and in a Grade A biosafety cabinet (BSC) monitored to Grade A environmental conditions, which is used for bioburden control. The techniques/operations, equipment, and environment for the activities observed were intended to control bioburden and maintain product integrity. The Company takes seriously the importance of effective procedures and controls in these areas. We have considered Observation 13 carefully and determined that our procedures and their implementation can be improved relative to filling of the purified (b) (4) prior to storage, as explained below.
Completed Actions:	Our actions in response to Observation 13 are in process.
Planned Actions:	We will implement a program to re-develop the procedures filling of purified (b) (4) for the filling operation to include: 1. The use of (b) (4) e.g., (b) (4) (b) (4) and/or **Target Completion Date:** March 29, 2019 2. The development and use of a manifold system for the filling and sampling of bottles eliminating the intermediary bag for receiving (b) (4) . **Target Completion Date:** April 30, 2019 3. A process engineer has been hired and a second process engineer is being recruited to focus on process improvements to enhance processing effectiveness, bioburden control, and containment of product. **Target Completion Date:** December 31, 2018 4. An experienced operations trainer, from upstream operations, will be reassigned to downstream operations to enhance our on-going training and educational initiatives. **Target Completion Date:** October 31, 2018 The net result of these four procedural improvements will be to reduce the risk of inadvertently introducing a microbial contaminate to the product. In addition, Immunomedics has retained microbiology and aseptic processing experts from (b) (4) to perform a comprehensive review of all ISO 5 aseptic processing operations. A formal report will be issued to Senior Management highlighting any key findings and improvement opportunities. Further improvements, wherever feasible will be established based on this continuous improvement initiative.

	Target Completion Date: October 31, 2018

Specifically, during a mock (b) (4) and dispensing of an (b) (4) intermediate surrogate conducted on August 9, 2018, the following was observed:

A. After (b) (4), the surrogate was transferred first to a single use (b) (4) L bag (SUB) and then from the SUB to (b) (4) The SUB was removed from its container and assembled in the Biologic Safety Cabinet (BSC) used for (b) (4) and dispensing. Multiple open-process manipulations were conducted to prepare the SUB, including (b) (4) (b) (4) to the SUB.

Response:	We acknowledge the deficiencies in the material handling in the BSC. We have assessed that the multitude of materials prepared, and activities performed in the BSC may have contributed to the observed actions.
Completed Actions:	Our actions in response to Observation 13A are in process.
Planned Actions:	The single-use bag activities observed will be moved to the BSC in room (b) (4) reducing the amount of materials and number of activities that occur in the BSC in room (b) (4) where the product is dispensed, and facilitating the actions/activities required to prepare the bag for use. **Target Completion Date:** September 28, 2018 Immunomedics has retained microbiology and aseptic processing experts from (b) (4) (b) (4) to perform a comprehensive review of all ISO 5 aseptic processing operations. A formal report will be issued to Senior Management highlighting any key findings and improvement opportunities. Further improvements, wherever feasible will be established based on this continuous improvement initiative. **Target Completion Date:** October 31, 2018 A review of SOP-0059: Use of (b) (4) and SOP-0063: General Cleanroom Guidelines and Practices will be conducted to enhance operations in the final bulk filling operation. Additional training on proper aseptic practices and (b) (4) operations in the BSC, will be conducted as indicated above. **Target Completion Date:** October 31, 2018

B. During the SUB preparation process, the end of the (b) (4) downstream the (b) (4) was observed to touch the operator's hands, the surfaces of the BSC and the material placed inside the BSC.

Response:	We acknowledge the deficiencies in the operator's aseptic handling of material in the BSC. Immunomedics is committed to training operators to ensure all operators involved in aseptic operations use proper techniques at all times as indicated above, and also take practical steps related to allocation of activities among available rooms to facilitate best practices. We have reminded our production staff and QA Supervisors that all aseptic operations should be monitored and observed by Production and/or QA on the floor personnel. Any potential compromise or poor technique that is observed will be noted as a deviation and referenced during the execution of respective batch production control records.
Completed Actions:	Our actions in response to Observation 13B are in process.
Planned Actions:	As noted above, the single-use bag activities observed will be moved to the BSC in room (b) (4), reducing the amount of materials and number of activities that occur in the BSC in room (b) (4) where the product is dispensed, and facilitating the actions/activities required to prepare the bag for use. **Target Completion Date:** September 28, 2018 As noted above, a review of SOP-0059: (b) (4) set-up and operation in the BSC and SOP-0063: Clean Room Practices will be conducted to enhance operations in the final bulk filling operation. Additional training on proper aseptic practices and (b) (4) operations in the BSC, will be conducted. **Target Completion Date:** October 31, 2018

C. Prior to filling the (b) (4) analytical samples were collected into (b) (4) The (b) (4) of the (b) (4) used to fill the (b) (4) and the (b) (4) are similar. In addition, the flow of the (b) (4) surrogate was not continuous and was difficult to control. As a result, the surrogate was spilled during the sampling process.

Response:	We acknowledge the deficiencies in the material handling in the BSC. We agree that the sampling equipment utilized made the filling operation difficult to complete in a controlled manner. Personnel have been retrained on proper techniques required to minimize the potential for spillage during the sampling process. In order to further reduce the microbial risks associated with the collection of analytical samples, the samples will be taken after most, if not all the product has been filled into (b) (4) As a longer term, preventative action, we are evaluating the feasibility of using a pre-assembled or manifolds with sample containers pre-assembled that facilitate the taking of analytical samples in a manner that is more closed.
Completed Actions:	Our actions in response to Observation 13C are in process.
Planned Actions:	The sample handling procedures and equipment will be modified to improve the controlled collection of samples, to reduce the likelihood of spillage or of contamination of either the samples or the (b) (4) intermediate. **Target Completion Date:** September 28, 2018

List of Attachments in Appendix B

	Document	483 Reference
1.	Ethical Conduct and Data Integrity Policy	#1
2.	Data Governance Program	#1
3.	(b) (4) Risk Assessment Summary	#2
4.	SOP-0148: Supplier Qualification Program	#4
5.	SOP-0698: GMP Raw Material Qualification	#4
6.	SOP-0185: Sampling of Raw Materials	#4
7.	GMP Warehouse Location Tracking Map	#5
8.	Deviation 18-053U (amended)	#10
9.	Protocol for Retrospective Review of Major and Critical Deviations and CAPA Relevant (b) (4) Intermediate Bulk PPQ Lots	#10
10.	SOP-0652	#10
11.	Immunomedics Quality Council Charter	#10
12.	(b) (4)	#12